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THE SIGNIFICANCE OF ALBUMINURIC RETINITIS IN PREGNANCY.

AN ANALYSIS OF FIVE CASES, WITH THE HISTOLOGICAL CHANGES PRESENT IN THE RETINA IN ONE CASE.

By Robert L. Randolph, M. D.

Two years ago I had my attention called to the importance of this subject by a case seen in consultation with Professor Kelly of the Johns Hopkins Hospital.

Case I.—Mrs. N., 31 years old; 3 children living, and up to the 4th month of her 3d pregnancy had enjoyed good health. In the early part of the 5th month of her 3d pregnancy she began to have violent headaches, which were almost constant, and they could only be relieved by strong anodynes. These headaches persisted for two weeks, when she noticed that her sight was growing dim. Her sight continued getting worse till it had reached a stage when, from her own account, she was practically blind in one eye and the sight in the other eye was but little better. At this time an oculist was called in, who pronounced it albuminuric retinitis and suggested an examination of the urine. This was done, and the urine was found to be rich in albumen, and casts were also found. The induction of premature labor was advised and performed, and the child was born dead. The woman had convulsions, but recovered, and in a few months was in comparatively good health again. Her sight was gradually but completely restored. One year later she again conceived, and about the 4th month of pregnancy was attacked with similar headaches, though they were not quite so violent in character. Fearing that her sight would become involved, she consulted an oculist, who, from the complete description he gave of the ophthalmoscopic condition, must have made a very painstaking examination. He came to the conclusion that she was suffering with the degenerative form of albuminuric retinitis, and that if she waited for normal labor she would unquestionably lose her sight and probably her life. Her family physician then sent her to Dr. Kelly, that he might induce premature labor, giving as the main reason the condition of the eyes and the prognosis held out by the oculist. The case was referred to me by Dr. Kelly for examination. I found that her vision was $\frac{20}{30}$ in both eyes, and that there was present in both eyes a low grade of hyperopic astigmatism. As to the condition of the fundi, I found absolutely nothing to denote a progressive disease. The fundi presented all over a granular stippling, with here and there the faintest suggestions of pigmentary deposits, such a condition as is not infrequently found associated with high degrees of myopic astigmatism. The question was whether or not to induce premature labor. I may add that she had a faint trace of albumen in her urine, but no casts. There was then, in my opinion, not the slightest suggestion of albuminuric retinitis, and had she not gone nearly blind at a previous pregnancy the question of inducing premature labor would never have arisen. From my examination, then, I concluded that the evidence did not justify the induction of premature labor. I saw no signs of a progressive retinitis, and viewing the condition of the retinæ exactly as they were, and entirely uninfluenced by the previous history, I told Dr. Kelly that, so far as her eyes were concerned, I saw as yet no reason for bringing on labor. My advice was followed and the patient sent home. A few months later her family physician wrote Dr. Kelly that she had given birth to a boy and had gone through an easy labor.

Case II.—Mrs. W., 26 years old. Married 11 months. Two months after seeing Case 1 I was called to see a case in consultation with Dr. T. H. West, of Keyser, W. Va., who told me the woman had been complaining of dimness of vision and violent headaches, but he

had not laid any special stress on the latter symptom, thinking it was due simply to indigestion incident upon her condition. She was in the 5th month of pregnancy. I found that with one eye she could count fingers across the room, but could not see to read; with the other eye she could read ordinary print. I had no test types with me and hence could not ascertain her actual vision. I found with the ophthalmoscope that the fundus in both eyes was covered with soft white patches. These white patches were nearly confluent in the worse eye, so that the fundus looked perfectly white. The patient had been in bed for nearly two weeks, as her nose would bleed every time she sat up or moved about. This nose-bleeding, then, was the only evidence of ill-health present, and until I gave my opinion as to the condition of the retinæ her physician had not thought of any serious disease. Her urine was immediately examined and found loaded with albumen; casts were also found. There was every reason to believe that the retinitis was progressing, and inasmuch as she had nearly four months before confinement, I felt justified in advising her physician to bring on labor. I was confident that the retina would be permanently destroyed if pregnancy were allowed to continue to full term. Dr. West induced premature labor, and the latter was easy, and a dead child was born. Her sight was gradually restored, and though I never had an opportunity of making an examination, I learned that a few months after her confinement she could see as well as ever. Her health continued delicate, and her urine was never free from albumen. Three months ago Dr. West told me that she was again in the 7th month of pregnancy and that her sight was becoming affected. She was very anxious for a child, and fearing that her physician would bring on labor, as he had done before, she had delayed revealing her condition. Her symptoms alarmed her and she sent for Dr. West late in the 7th month. At this time she had some local dropsies, very noticeable about the labia majora. The urine was rich in albumen, and her sight growing worse every day. I advised premature labor at once, and expressed some doubt whether sight would be saved, as she had undoubtedly gone too long. Her labor was an easy one and the child lived three days. Since Saturday, April 14th (Dr. West writes me), she can no longer see a person across the room.

Case III.—A. H. (colored), 26 years old. Has three children. Married five years. One miscarriage. Just before birth of second child she noticed dimness of sight. This disappeared, and her attention was not attracted to her eyes till she was four months advanced in her 3d pregnancy. Her sight grew worse every day, and all this time she suffered with the most violent and persistent headaches. Her child was born, and four months afterwards she came to the Dispensary of this Hospital. The following was the condition of her eyes: R. E. $V=\frac{1}{200}$; L. E. $V=\frac{2}{200}$. Both fundi were beset with large white plaques. In the right eye there were some opacities in the vitreous, and the optic nerve was pale. The white spots were confluent in the macula region, forming a solid white background. I found a similar condition, somewhat less marked, in the left eye, the optic nerve in this eye not being involved. The diagnosis of albuminuric retinitis was readily made. I examined the urine and found a quantity of albumen, and also casts. She was referred to the medical side of the Dispensary. She died very suddenly a few weeks later, and I succeeded in getting one of the eyes, which I hardened in Müller's fluid and studied the histological changes.

Case IV.—Mrs. S., 32 years old. Has two children. When I first saw her she had just recovered from her 2d pregnancy, when she said she had nearly lost the sight of her left eye, and the other eye was also affected. I found evidence of retinitis in the left eye. There were very minute white specks with pigmented borders collected in the macula region, also some spots of pigment in the same locality. Her vision in this eye was $\frac{2}{70}$. In the other eye, vision was $\frac{2}{20}$. I prescribed glasses for her (I may add she had a slight grade of hyperopic astig., and had come to me for headaches), and lost sight of her for 18 months, when she returned with the request from her family physician, Dr. Gombel of this city, that I examine her eyes. She was in the 4th month of pregnancy, and fearing that she would lose her sight if she went on to full term, her physician sent her to me and told her that he would induce premature labor if I thought her eyesight was in danger. She was very poor, and I soon found out that neither she nor her husband wished for more children and were exceedingly anxious for a legitimate excuse for getting rid of the fœtus. I examined her eyes most carefully and found no difference in the condition from that seen some months before. There was no change in either the subjective or objective condition, and I did not think that this justified the immediate induction of labor, and so wrote to Dr. Gombel, who refused to bring on labor. She was determined, however, to have her pregnancy terminated, and four weeks later, Dr. Gombel tells me, he was called in and found her moribund with peritonitis. She had sent for a midwife, who had produced abortion that resulted in her death.

Case V.—Mrs. R., 40 years old. Has had eleven children, and is now in the 5th month of her 12th pregnancy. Ten days ago noticed that the sight in her left eye was very dim, and that she did not see as well as usual with her other eye. She had been troubled with a great deal of what she called "neuralgia of the head." This condition grew rapidly worse, especially in the left eye, the right eye remaining unchanged. When seen at the Dispensary of the Johns Hopkins Hospital she looked pale and waxy, and I elicited the fact that her feet were somewhat œdematous. Her vision in the left eye was reduced to counting fingers in three feet, and in the right eye vision was $\frac{20}{30}$. Ophthalmoscopic examination showed large white patches around the optic nerve in the left eye. The entire retina looked pale, and the outlines of the disc were blurred. No noteworthy changes in the blood-vessels. There were several small patches in the macula region. The right eye showed three small white plaques near the optic nerve; further than this, nothing abnormal. I diagnosed the condition albuminuric retinitis, and had an examination made of her urine. This was found to contain slightly over $\frac{3}{10}\%$ albumen, and granular casts were also present. There was then no doubt about the gravity of her condition, and I advised the induction of premature labor as the only means through which she could regain her sight. I have not seen her since, but have learned that both she and her husband concluded to have nothing done and to wait and see "if nature would not bring things all right." I shall inquire into the case four months hence.

What were the prominent symptoms that characterized the histories of these five patients? In the first three and last case the dimness of sight and headaches. In these cases there was not the slightest suggestion of kidney trouble outside of the ocular complication, and it was this latter condition that alarmed the attending physician and finally led to the discovery of more imporant and far graver conditions. It is clear then that much weight should be attached to dimness of sight occurring at any time during pregnancy.

In looking over the literature of this subject one will be disposed to divide the albuminuric retinitis of pregnancy into two classes: 1st, those cases where the eye symptoms appear before the 6th month; 2d, those cases where the eye symptoms appear later than the 7th month. I should place cases I, II, III and V in the first class, and case IV in the second class.

Retinitis albuminurica in its relation to pregnancy is certainly worthy of more than a passing notice, and yet in the majority of obstetrical works there is no special warning to

the physician to heed all symptoms of visual disturbance, nor is even the special gravity of the condition mentioned. It is surprising to see how much has been written in this connection by ophthalmologists in the past ten years, and how in every case reported what serious conditions were present. From remarks let drop to me in talking over the cases with others, I am led to think that at least one case of eclampsia falls to the lot of most practitioners, and I think that were it possible to get the complete history of the pregnancy of eclampsia cases, in a large number eye symptoms more or less pronounced were present at some time during pregnancy, and generally in the earlier months, and it is just at this point, when the eye symptoms manifest themselves, that a serious view of the case should be taken. In the cases reported by other observers the physician in charge became alarmed at the first suggestion of eye trouble, and had an ophthalmoscopic examination made at once. It should be remembered that failing sight is often the first indication that the woman's health is failing, and is the first symptom to which she calls the doctor's attention. The retinal lesion is often the index of the systemic condition, and the slightest disturbance in sight may mean just such a lesion; and while other signs, such as large quantities of albumen in the urine, the presence of granular and hyaline casts, and œdema of the feet, are probably indispensable for a diagnosis of nephritis, these latter conditions will almost certainly be found in the pregnant woman whenever the ophthalmoscope reveals the changes in the retina known as albuminuric retinitis. But even the absence of the more obvious signs of nephritis should not lead us to underrate the significance of the retinitis, for Howe reports a case where both retinæ in May presented the typical picture of albuminuric retinitis, and where an examination of the urine during the course of four months failed to reveal albumen, and it was not till September that albumen was found, and then in considerable amount; a fact which, I think, enhances the importance of an ophthalmoscopic examination. In Case I, vision was nearly extinguished at a previous labor. As a general thing, after such an experience, the family physician warns his patient against the dangers of becoming pregnant again, as the history of most cases goes to show that with every succeeding pregnancy greater inroads are made upon the integrity of the retina. The 1st and 4th cases reported would seem to show, though, that it is quite possible for a woman who has been nearly blind from renal retinitis at labor to go through her next pregnancy without the slightest return of the eye trouble. When such cases as cases I and IV present themselves to the oculist for an opinion, unless there be evidences of an existing disease in the retina, the question of premature labor from the ocular point of view is not to be considered. Such a case should of course be returned to the obstetrician, who will be guided by other signs.

I followed this course in cases I and IV, and subsequent events verified my opinion. On the other hand, as regards cases II, III and V, there was not the slightest doubt in my mind that unless pregnancy were terminated at once blindness would follow. A retina that was so evidently diseased in its entirety would surely be destroyed if the conditions that gave rise to this disease were allowed to remain three or four months longer. Howe's statistics in these cases, when labor was not induced, show that when the woman escaped with her life it was only to remain blind forever afterward.

In those cases where the retinal trouble manifests itself in the last seven weeks of pregnancy we may give a more favorable prognosis, and unless the retinal lesion be very pronounced and the quantity of albumen great, hesitate before advising the induction of premature labor. The later the renal retinitis makes its appearance the more favorable the prognosis as regards sight, and when showing itself in the last two weeks of pregnancy, recovery of sight follows almost invariably.

1. Visual disturbances occurring in the first six months of pregnancy, and especially when associated with violent headaches, frequently mean albuminuric retinitis, and if this condition is found, to save sight, pregnancy should be at once terminated.

2. Visual disturbances showing themselves in the last seven weeks of pregnancy, while indicating the same retinal lesion, are of less grave import in so far as sight is concerned, and unless these disturbances are very pronounced and associated with wide-spread ophthalmoscopic changes, should not in themselves call for the induction of premature labor, for here their history goes to show that sight is completely restored after labor. This is especially true when the retinitis shows itself in the last two weeks of pregnancy.

3. The occurrence of renal retinitis in one pregnancy does not mean that the woman will be likewise affected in a subsequent pregnancy, and even though headaches be present and albumen found in the urine, so long as the fundi are free from the usual signs of an existing albuminuric retinitis the question of sight should not properly be considered.

PATHOLOGY.

Denissenko denies the existence of an inflammatory exudation, and regards the retinal changes as merely œdematous, and proposes to substitute the name of ophthalmia Brightica or œdematosa, for that of albuminuric retinitis. Holsti, who has investigated the subject, says that the affection comes from inflammation of the coats of the arteries, and that the walls are changed into a shining homogeneous mass resembling colloid degeneration. Maguire holds that the changes are degenerative in character and due to excessive intravascular tension, and that this alone will cause the hemorrhages and nutritive disturbances. Weeks thinks that the alterations are of a fibroid or hyaline nature taking place in the blood-vessels.

Duke Charles Theodore of Bavaria found that arteritis was very common in the retinal affections of Bright's disease, and that the chief changes are in the capillary layer of the choroid and in the retina, and more in the former. The coats of the larger vessels in the retina present a waxy structure; in other parts are homogeneous. Small aneurisms may be present and hemorrhages into the sheath of the vessel. The inflammatory process is specially well marked in the capillary area between small arteries and veins. There is thickening of the vessels associated with degeneration of red and white blood corpuscles

and by œdematous swelling of the walls. The lumina are sometimes narrowed, and thromboses occur. There is an infiltration of the rods and cones by small cells, and the formation of hyaline masses in the granular layers. He did not find traces of sclerosis of nerve fibres. The arteritis is seen in vessels of the sclerotic, ciliary body, iris and conjunctiva.

Diffuse opacity of the retina is mainly due, says Saundby, to œdema, the lymph spaces around the ganglion cells of the nerve-fibre layer being distended with a clear fluid, so that these drop out of the section, leaving large spaces. We may have an effusion of coagulable lymph in the outer molecular layer, or such an exudation may separate the membrana limitans externa and bases of Müller's fibres from the rest of the nerve-fibre layer, while the layer of rods and cones may show great thickening. Small angular spots of pigment appearing in the periphery are of less importance, and are due to changes in the pigment epithelium. Sometimes, says Saundby, choroidal hemorrhages may occur, giving rise to atrophy of the choroid at this spot and pigmentary disturbance. Hemorrhages, the same author writes, occur in the sheaths of the retinal vessels. Interstitial neuritis is sometimes seen with round cell infiltration of the connective tissue of the nerve, leading in some cases to atrophy of the nerve. Ivanoff found a serous transudation into the retina in the immediate vicinity of the blood-vessels, and thinks that the outer coat of the vessels and not the inner coat is affected.

Pathological Histology in Case III.

As regards the optic nerve itself, I think we may safely say it was normal. There might have been increased nucleation in the papilla, noticeable in and about the perivascular spaces. The main point of interest here was a beautiful endarteritis of the central artery, not amounting to obliteration, but to a considerable narrowing of the lumen of the vessel. One saw here what some authors speak of as fibrous thickening of the intima. The central vein was engorged with red blood corpuscles, a condition peculiar to the veins everywhere throughout the sections and in every part of the eye. The choroid was normal with the exception of the condition of the veins just mentioned. In the retina marked and interesting changes were present. The layer of rods and cones was absent in places, a loss due, doubtless, to mechanical violence in the preparation of the specimen. The membrana limitans externa was possibly somewhat thickened, and had a wavy course due to the pressure from the swollen inner layers. The external granular layer was increased in depth and the cells were pressed apart. Further than this there was an absence of any histological change in this situation. The external molecular layer showed marked changes—1st. The fibres of Müller were swollen and pressed apart, and in some places there were large spaces, the latter being filled with disintegrated blood corpuscles, hyaline masses, and sometimes distinct fibrillated fibrin. The walls of these spaces were lined with very fine drops of hyaline material. Fibrin in no inconsiderable amount was also present generally in that part of the layer between the spaces. Some of the smaller spaces were blocked up with hyaline masses. Here and there were small hemorrhages. At some points the spaces were so large as to invade the external granular layer. The internal granular layer presented, in the main, changes similar to those in the external molecular layer, except that there was an absence of the spaces seen in the latter. The internal molecular layer, ganglion-cell layer, and nerve-fibre layer presented noteworthy changes. At points there was an enormous increase in the neuroglia (sclerosis), and this was especially marked in the nerve-fibre layer. The fibres in this layer were swollen and somewhat translucent. This sclerosis was more pronounced in certain spots; spots no doubt corresponding to the location of the white patches seen with the ophthalmoscope. These spots of sclerosis appeared like nodes, involving all the layers of the retina down as far as the internal granular layer and almost destroying the identity of the layers as such. The nerve-fibre layer was thickened throughout, and minute hemorrhages were visible. The ganglion-cell layer presented peculiar changes. Adjacent to and within the nodes the cells were frequently absent, having dropped out of the section, leaving vacuoles. When present, some of them were much enlarged, some were smaller than normal, others without processes. With eosin-hæmatoxylin stain some of them presented a brownish red and rather singular color. The relatively great size attained by the ganglion-cells is, according to Weeks, brought about by imbibition, a part of the general œdema. Small hemorrhages and hyaline drops were present in the internal molecular layer.

The principal features then were:

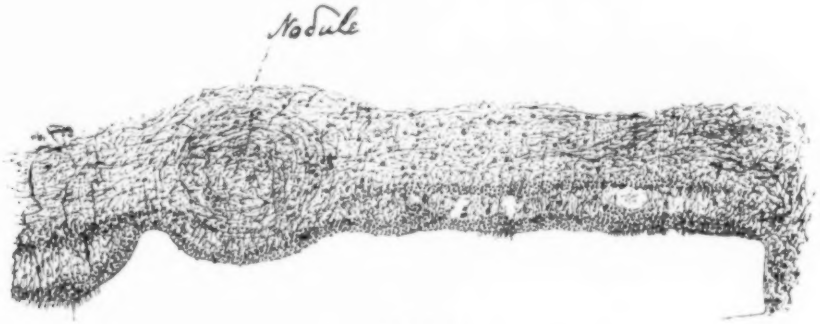
1st. Great œdema of the entire retina, and as a consequence increased depth of the retina.

2d. Hyperplasia of the neuroglia, especially marked in the nerve-fibre layer.

3d. The presence of hyaline masses throughout the retina, most pronounced in external molecular layer and the formation of spaces.

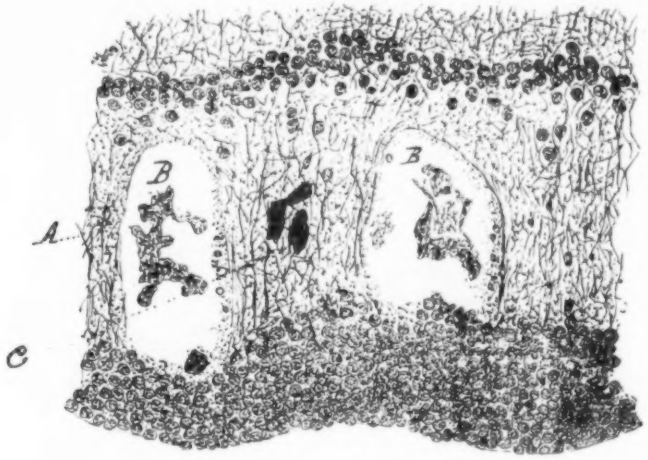
4th. As a general thing the changes were more striking the nearer the disc, and this was especially true of the nodules, which here were very prominent, though they were visible along the retina almost as far forward as the ora serrata. The anterior portion of the eye was normal. Fatty degeneration of Müller's fibres observed by Leber and Duke Charles Theodore was not seen in this case, though the failure to find this condition does not disprove its existence. Müller's fluid was employed in hardening the eye, and this could account for the failure to detect the changes described by Leber and others, and in like manner post-mortem changes may be held responsible.

As to the frequency of sclerosis of the neuroglia in albuminuric retinitis, I am disposed to regard it as of exceptional occurrence—if ever present at all—when pregnancy alone not associated with genuine interstitial nephritis is the cause of the albuminuria. It is frequently difficult to ascertain the subsequent history of this class of patients, but whenever the eyes have been tested some months after premature labor, in most cases useful vision was present, and there was good reason to believe that vision would still further improve. In some few cases nearly normal vision has been reported. Anything like restoration of function in a part the subject of sclerosis is certainly not in accord with our ideas of this process, as witness for example the prognosis of the same condition when present in the cerebro-spinal system, in which latter connection Flint says, "Clinical experience thus far has furnished no ground for entertaining any hope of recovery from the disease." The blindness, then, which is present in albuminuric retinitis is due to œdema of the retina, and consequent interference with the conductivity of the nerve-fibres. This œdema may be in many cases a part of the general œdema familiar to us all, an œdema which usually disappears with the removal of the fœtus. The sclerosis found in Case III leads me to conclude that the nephritis at the last was not of the parenchymatous variety, as are most of the cases of nephritis of pregnancy. The disappearance, however, of the visual disturbances and headaches at the termination of her



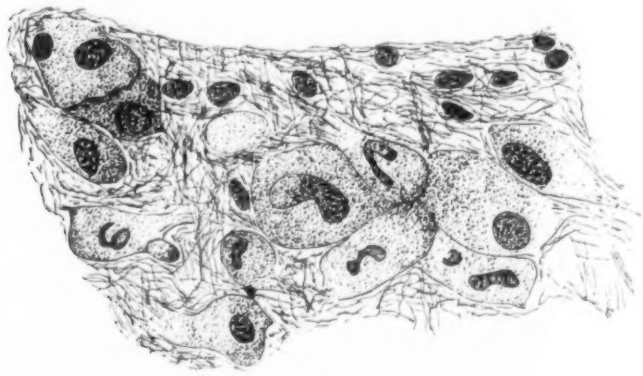
No. 1.

Showing how one of the nodules has invaded the retina as far as the Internal Granular Layer, and has destroyed the identity of the layers involved.



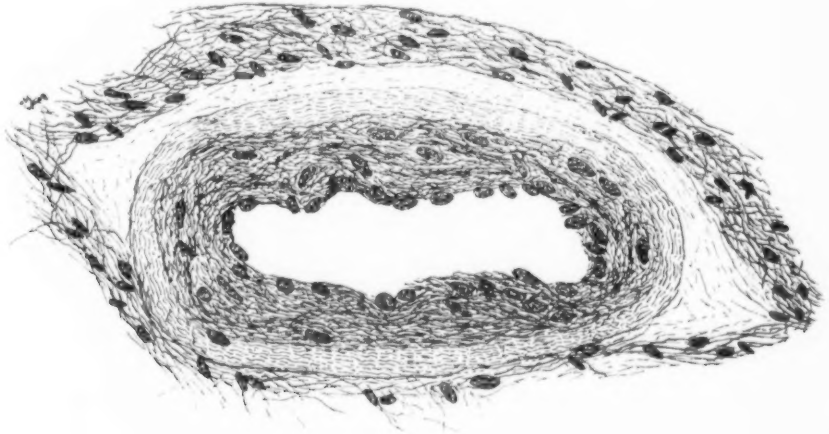
No. 2.

A, External Molecular Layer.
B, Spaces in External Molecular Layer filled with hyaline masses, fibrin.
C, Hyaline masses.



No. 3.

Swollen Ganglion Cells in Ganglion Cell Layer.



No 4.

Endarteritis of the Central Artery.

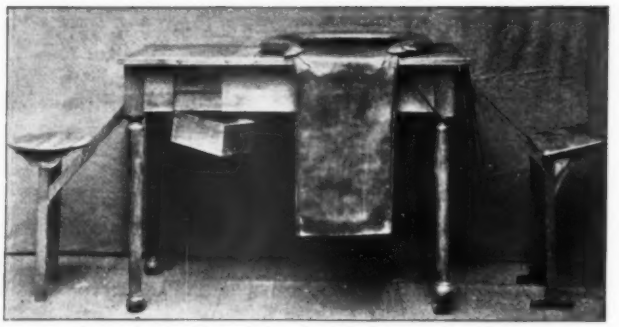


FIG. 1.—Modified Operating Table for Abdominal Section.

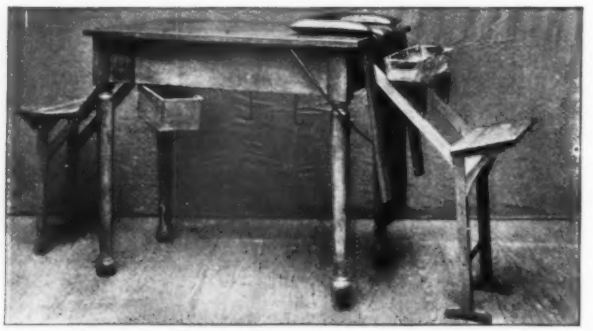


FIG. 2.—Modified Table for Plastic Operation.

FIG. 3.—Modified Operating Table, Trendelenburg Position.

second pregnancy speaks in favor of a parenchymatous nephritis in the early part of her history; a nephritis that in exceptional cases, as in this one, passes over into the interstitial variety; a condition that we no doubt had here, as evidenced by her sudden death, and by the clinical history of the retinitis, as well as its histological changes.

LITERATURE.

Abortion for the Albuminuric Retinitis of Pregnancy. By Lucien Howe, M. D. *Amer. Jour. Ophthal.*, 1886, No. 2.

Albuminuric Retinitis during Pregnancy. By Theodore Maxwell, M. D. *The Lancet*, 1878, Vol. 2, p. 900.

Ein Fall von Retinitis albuminurica mit hochgradige Netzhautablösung während der Schwangerschaft entstanden. Von H. Buch in Berlin. *Archiv f. Ophth.*, 2. Abth., 102–114.

The Prognosis as to Life in Renal Retinitis. By Simon Snell. *Trans. Oph. Soc. of United Kingdom*, Vol. VII, 1888.

Another Case of Albuminuric Retinitis of Pregnancy. By A. D. Williams, M. D. *St. Louis Med. and Surg. Jour.*, 1887.

Albuminuric Retinitis. Its Dangers and Diagnosis. By A. D. Williams, M. D. *St. Louis Med. and Surg. Jour.*, 1887.

Retinitis Albuminurica during Pregnancy. Premature Labor with Improvement of Vision. By W. O. Moore, M. D. *The Planet*, 1883-84, I.

Albuminuric Retinitis without Albumen. By Lucien Howe, M. D. *Trans. of M. Society, State N. Y.*, 1893.

Gravidität in 8. Monat. Beiderseitige Retinitis albuminurica mit Netzhautablösung. Von Dr. Hester. *Charité-Annalen*, 2. Jahrgang.

Retinitis Albuminurica. Improvement after Premature Labor. By C. Macnamara. *The Lancet*, 1878, Vol. 2, p. 842.

Retinitis Albuminurica and Pregnancy. By Frank Van Fleet, M. D. *N. Y. Med. Jour.*, Sept. 26, 1871.

Albuminuric Retinitis. By A. Emrys-Jones, M. D. *British Med. Jour.*, April 14, 1883.

Two Cases of Severe Albuminuric Retinitis coming on during Pregnancy. Recovery of health and good sight in both eyes after miscarriage in one and artificial premature labor in other. *Oph. Hosp. Reports*, Vol. II, 1886–88.

The Middlemore Lectures on Retinal Affections of Bright's Disease and Diabetes. By Robert Saundby, M. D., F. R. C. P. *Birmingham Med. Review*, Jan. 1893.

A Contribution to the Pathology of Albuminuric Retinitis. By Dr. John E. Weeks of N. Y. *Archives of Ophth.*, Vol. XVII, pp. 276–291.

Zur path. Anat. des Auges. By Duke Charles Theodore. Wiesbaden, 1887.

The Changes in the Eye in Bright's Disease. By G. Denissenko. *Med. Westnik*. 1882, Nos. 49 and 50, and 1883, Nos. 2 and 11.

Ueber die Veränderungen der feinen Arterien bei der granulären Nierenatrophie und deren Bedeutung für die pathologischen Krankheiten. Von H. Holsti. *Deutsch. Archiv für klin. Med.*, XXXVIII, p. 122.

Traité des Maladies des Yeux. Ivanoff (A.). *Conf. Wecker*, t. II, p. 316.

AN OPERATING TABLE.

BY HUNTER ROBB, M. D., *Associate in Gynecology.*

[*Read before the Johns Hopkins Hospital Medical Society, May 21, 1894.*]

I have recently had made an operating table which is a modification of the one devised by Dr. Kelly, which you have all seen in his operating room. It is made of quartered oak and is 80.5 cm. high. The top, which when complete measures 110 cm. by 51.5 cm., is constructed in three separate pieces, which, for convenience, I will call *A*, *B* and *C*. The middle portion, *B*, measuring 15 cm., is made like an extra leaf of a table to slip in and out, so that when required the table can be at once shortened by joining *A* and *C*, so that the top consists only of these two parts. This allows the anæsthetizer to administer the anæsthetic during an operation on the cervix or perineum with the patient in the lithotomy position, without leaning forward in a constrained position, as he is obliged to do when the ordinary table is employed (Figs. 1 and 2). The part *C*, again, consists of two pieces which are joined together by hinges. The part which works on these hinges can at any time be elevated at any angle and kept in the required position by means of a wooden support 11 cm. wide and 48.5 cm. long, one end of which is attached to the table on its under surface by a double hinge, while the other can be fitted into a series of grooves in a plank which lies a little below and parallel to the top of the table. In this way we have a simple apparatus when we wish to employ the Trendelenburg position (Fig. 3). The legs of the patient when in this position rest upon a support which is attached to the elevated portion of the table at a convenient angle. Instead of being made in one piece, the middle portion of this support, which is 30 cm. long and 30 cm. wide, is constructed to fit into grooves in the two projecting side-pieces, so that when it is no longer required it can easily be removed. This is necessary, because if left in place it would obstruct the lowering of the table when a horizontal surface is required.

The support for the feet of the patient, when undergoing an abdominal operation, can be used as a seat for the operator when he is engaged in plastic work. In the two pieces of wood which connect the seat with the table, holes are drilled which are intended to receive two pegs, the tops of which are represented by two triangular pieces of wood. When in position they can be used to support a glass basin, which thus rests just in front and within easy reach of the operator, and into which can be put the scissors, knives and any instruments which are constantly being required during a plastic operation. This seat, as well as that for the anæsthetizer, can be put out of sight, being suspended under the table at any time when not in use. The legs of the table at one end are supplied with rubber casters, so that the position of the table can be readily changed.

A wooden box is fastened on the under surface at the side of the table near the head, in which are kept the anæsthetic, cones, hypodermic syringe and other things that may be required during the operation by the anæsthetizer.

The advantages which the table possesses are as follows:

(1) it is inexpensive; (2) it can be readily sterilized; (3) it can be shortened at a moment's notice; (4) the patient can easily be placed in the Trendelenburg position at any time, even in the middle of the operation, without being removed from the table; (5) the seats for the operator and the anæsthetizer, when not required, are out of the way; (6) a convenient receptacle for some of the most necessary instruments is put within easy reach of the operator; (7) a box is supplied to hold the ether, chloroform and cones; (8) the table can readily be wheeled from place to place.

PRIMARY CARCINOMA OF THE GALL-BLADDER.

By Delano Ames, M. D.

[*Read before the Johns Hopkins Hospital Medical Society, May* 21, 1894.]

About one year ago the first case that I shall report this evening came into my care through the kindness of Prof. Osler, to whom I am also indebted for the histories of the two other cases reported, which occurred in this hospital.

Case I.—*Primary carcinoma of the gall-bladder. Pain and tumor in the right hypochondrium. Absence of jaundice. Profound anæmia. Obstinate constipation for four weeks before death. Death from exhaustion six days after exploratory incision. Gall-stones.*

Miss R. H., aged 47, was in my care from May 5, 1893, to Jan. 15, 1894. She had been an invalid for some years. Her mother is said to have died from some painful liver trouble. Her previous health had never been of the best. Since childhood there is a history of attacks of pain in the right side, occurring with increasing frequency as she grew older. She never was jaundiced during these attacks and never passed calculi. She always menstruated regularly, never freely, and for the last few years has suffered more or less pain in the left inguinal region during the menstrual period. Two years ago, during a severe attack of pain in the right side, she first noticed a slight swelling just below the right costal margin in the mammary line. This subsided with the pain. The duration of these attacks was from six to eighteen hours.

Aside from this trouble, and with the exception of a troublesome cough, for which she sought the climate of southern Europe two winters ago, she had been free from disease.

Her appetite was only fair at all times. Her bowels moved from 2 to 3 times a day.

On my first visit, May 5th, I made the following note: "Patient is fairly well nourished. Complexion sallow. No jaundice. Conjunctivæ are colorless. Mucous membranes of mouth are very pale. Ears waxy. Pulse 84, volume and tension good.

Thorax:—Fairly well developed. There is a small amount of subcutaneous fat. Expansion good, but apparently slightly restricted at left apex, where the expiration is somewhat prolonged. No râles are to be heard. Heart negative.

Abdomen:—Soft. Walls are thin. Just below the right costal margin the surface is a little elevated in a small area in the mammary line. There is tenderness here to slight pressure, and she tells me that yesterday when the pain was more acute this elevation was more marked. Liver dullness begins at the 6th rib. The border is palpable about two fingers-breadth below the costal margin and is painful to pressure. The surface is smooth and firm. The left lobe is not palpable." The urine examined a few days later was free from albumen and casts, but showed slight traces of biliary coloring matter. Hæmoglobin was not estimated at this time, but three months later, after the patient had been in the country all summer, it was between 28 and 30 per cent.

A few days later the slight elevation noted on my first visit was found to be much accentuated and to be extremely sensitive to pressure. The patient was having a severe attack of pain in the right side.

Dr. Osler saw the case at this time and believed it to be probably one of chololithiasis of long standing, with adhesions of the gall-bladder to surrounding parts; the recurring attacks of swelling and pain in the region of the gall-bladder being referable to intermittent obstruction of the cystic duct. Operative interference was not advised on account of the patient's anæmic condition.

From September until December the patient's condition remained practically stationary, but from the latter date she began rapidly to grow worse, having several severe attacks of pain in the former place within a short time. During one of these attacks her temperature rose to 101°, but quickly subsided. After the attack the liver border was found to be somewhat lower than on the first examination. With the pain, as with all previous and all subsequent attacks, there was a slight menstrual flow and pain in the left inguinal region. This latter pain always accompanied defecation, and was increased if the stools were loose or the action constipated.

Although from this time the patient grew steadily worse, her appetite improved and there was no noticeable emaciation. Another marked change occurred; instead of having from 2 to 3 stools a day she suddenly and without apparent cause became obstinately constipated.

An examination made the middle of December showed the liver border palpable on a line with the umbilicus. The left lobe was still not palpable. There had thus been a noticeable descent of the right liver border in a short time.

On Christmas day occurred the most severe attack of pain yet experienced. The whole right hypochondrium was distinctly bulged; the liver border was 1 to 2 fingers-breadth below the umbilicus, and beneath it could be felt a rounded mass, which by bimanual palpation, one hand in the flank and one over the liver border, could be slightly moved up and down. It was not possible to make out any fluctuation. There was great tenderness, not only at the liver border, but over the whole liver surface. Twelve hours later the bulging was much less perceptible, the pain had gone, though some tenderness remained and the liver border was again on a level with the umbilicus.

Within eight days a second similar attack occurred, at which time it was decided that operative interference was advisable, as all the symptoms pointed to a probable occlusion of the cystic duct. An incision was therefore made by Dr. Tiffany on January 9th. The gall-bladder was found to be the seat of a cancerous growth and to be firmly adherent to surrounding parts. The patient died six days later from exhaustion.

The autopsy was made the following day at the bedside, and as we were not allowed to remove the organs, the report is far from being as full as would be desired.

The gall-bladder was enlarged to about the size of a large orange. It was dark brown in color; its walls were much thickened and the seat of a carcinomatous growth. On section, its cavity, which was small, contained a little brownish fluid, mushy detritus, and what was of most interest, the disintegrated remains of several gall-

stones. The mass was adherent to the duodenum for several inches below the stomach. It was also adherent to the under surface of the liver, and had, as it had grown, drawn down a tongue-like process of liver tissue in the way recently described by Riedel.

The liver, so far as could be seen, was free from secondary deposits, though it is very probable that a closer examination would have disclosed some metastatic nodules, as invasion of the liver in these cases is very common.

There was no constriction of the intestines. The lumen of the duodenum was normal. No growth was found at the pylorus or in the pancreas. The left ovary was cystic, about the size of a walnut and adherent to the rectum. This fact probably explains the pain in the left inguinal region referred to.

CASE II.—*Cancer of the gall-bladder. Jaundice. Progressive emaciation.*

E. S., aged 54, female, admitted to ward G, January 25, 1893, complaining of pain in the abdomen and of soreness in the back. There is nothing of moment in the family history. She has been married, has had six children and four miscarriages. Has never had uterine trouble, and no serious illness until the present attack.

More than a year ago she had quite severe pains in the back accompanied with high-colored urine. After several of these attacks she passed small calculi in the urine. She has had none of these attacks and has passed no stones for about a year. For the past few months she has been failing in health, has had indigestion, belching, and occasional attacks of vomiting. She has lost much weight. About five weeks ago she noticed that she was growing yellow, and for about the same length of time she has had a dull aching pain in the right side of the abdomen. The urine has been high-colored, and the stools, formerly dark in color, have been light gray.

Present condition:—Patient is a medium-sized woman, face is thin, but the body and limbs are still well nourished. There is a moderate jaundice. Abdomen is full. On palpation it is soft, nowhere painful except at a point 5 cm. below the costal margin in the nipple line. Here is a firm mass which extends to the left to within 6 cm. of the umbilicus, and at this border the fingers can be placed directly beneath it. Below it reaches to the transverse navel line, and is here rounded and the finger cannot be placed beneath it so well. To the right the margins are not very clearly defined, but the mass extends nearly to the tip of the 10th rib. Above it cannot be separated from the liver. It feels like a rounded mass the size of a lemon or a little larger, is extremely resistant, hard, and though it has the situation of the gall-bladder, scarcely conveys the impression of the rounded pear-shaped outline of that organ. The right kidney cannot be felt. The mass, though directly continuous with the liver, presents a flat tympany on percussion. Deep pressure from behind in the flank presses the mass forward.

The spleen is not enlarged, stomach not dilated, the pelvis is clear. The urine is dark-colored and there are a few granular casts. The stools are clay-colored and very offensive. Repeated examinations showed essential changes in the condition of the tumor mass. The jaundice became very much more intense, though the general symptoms were somewhat ameliorated. She took her food better and had much less pain. The case was regarded as tumor of the gall-bladder associated with gall-stones and probably malignant disease. The patient's condition was so satisfactory that it was thought advisable to have an exploratory operation to determine the exact nature of the trouble. Therefore, on February 8th Dr. Halsted made an exploratory incision. The mass described was in the position already referred to between the transverse colon and the under surface of the liver, to which it was firmly adherent. The adhesions to the colon were so tight it was thought inadvisable to attempt to separate them. The tumor mass was firm, solid, and grayish white in color; it passed beneath the surface of the liver and occupied the position of the gall-bladder. The liver itself was not enlarged, but the edge could readily be felt about 6 cm. above the lower border of the tumor mass.

The wound healed, but the jaundice persisted and she got progressively emaciated. Her friends took her home on March 2, where she subsequently died.

CASE III.—*Persistent jaundice with emaciation and ascites. Nodular tumor at the edge of the right liver lobe.*

Magdelen H., aged 52, admitted to ward G, October 18, 1892, complaining of swelling of the abdomen and legs.

Her father died of tuberculosis. No history of cancerous disease in the family.

The patient has always been a very healthy woman; was married at 22 and has had one child. Has been troubled for many years with constipation. She has never had attacks of colic.

The present illness, dating from the middle of June, began with vomiting, after which she became yellow and had an itching of the skin. The jaundice has never entirely disappeared. The legs became swollen about the end of August, and the abdomen six weeks ago. There has been pain in the back so that she always has to lie on the side; otherwise she has not much distress. The stools have been yellow. She has had but little vomiting. There has been progressive loss of flesh and strength.

Present condition:—The patient is much emaciated and has an intense olive-green jaundice. There is general anasarca. The abdomen is extremely distended and the lower zone of the thorax is expanded. Without going into details foreign to the main point, it may be said that she had all the signs of obstructive jaundice and an ascites which required frequent tapping. The immediate interest in the case was in the condition of the liver. After tapping, this was distinctly palpable, and in the parasternal line the rounded edge could be clearly felt about two fingers-breadth from the costal margin. Passing towards the flank in the anterior axillary line a prominent nodular mass was reached, and here the liver border was nearly 7 cm. below the costal margin. The mass felt about the size of a walnut, was prominent, not umbilicated. No other masses could be felt, but the edge of the liver in the parasternal line was somewhat irregular.

Autopsy:—This showed a primary carcinoma of the gall-bladder, the end of which was the nodular mass which was so definitely felt on palpation. The walls were greatly thickened and the bladder contained about 100 small stones. There was great induration about the common duct, the head of the pancreas and in the gastro-hepatic omentum. The common duct passed through this mass and was almost occluded. The liver weighed only 1500 grammes, and presented numerous medium-sized cancerous nodules throughout its substance.

In all these cases, but especially in the first and third, it was difficult to make an exact diagnosis from the symptoms and signs. In Case I, although all the symptoms pointed to trouble about the gall-bladder, there was no jaundice, and though malignant disease was thought of, the diagnosis of cancer was not made because of the absence of cachexia and emaciation. One point in favor of the diagnosis of cancer was the profound and obstinate anæmia, the hæmoglobin never registering above 28 to 30 per cent. The case was regarded as one of long-standing chololithiasis until the operation showed the presence of a neoplasm.

The chief points of interest about the case were: the rapidity with which the unfavorable symptoms developed; the rapid apparent increase in the size of the right lobe of the liver while the left remained normal; the intermittent swellings in the right hypochondrium; the absence of jaundice, cachexia and emaciation; the presence at autopsy of apparently disintegrating gall-stones.

In Case III the persistent jaundice and loss of weight suggested a new growth, but whether in the stomach, in the pancreas or in the liver, it was almost impossible to say. A test breakfast showed free hydrochloric acid, and she had not much vomiting since admission to the hospital. The stools were grayish yellow, not fatty, and not suggestive of pancreatic disease. The nodular body at the right border of the liver was the main objective point in the examination, and the question was discussed—before the class—as to whether this was a secondary growth, or the projecting end of a firm, hard cancerous gall-bladder. Supposing it to be secondary cancer of the liver, the organ was not nearly so enlarged as is common in this condition at the end of five or six months. On the other hand, in primary cancer of the gall-passages the liver is not so enlarged, and the jaundice, as in this case, is intense from the outset. A point in favor of this view was the absence of evident signs of disease of the stomach, pancreas and intestines.*

At the best, carcinoma of the gall-bladder is not very easy to recognize, but in doubtful cases there are certain points with regard to sex, age, and the previous history of the patient that sometimes will assist us in making a diagnosis.

Historical.

The literature of primary carcinoma of the gall-bladder is all of comparatively recent date; the most important contributions having been made within the last five years. By far the largest number of cases have been reported since 1870. To-day cases are constantly appearing, especially in the clinics of large hospitals, and we are beginning to regard as not uncommon a disease that has hitherto been considered rare. There is reason to believe, however, as Ranvier and Fagge have pointed out, that a number of these cases are still overlooked, especially when there are large cancerous deposits in the liver, such being too hastily regarded as primary in that organ.

Previous to the year 1800, I have been able to find records of but four cases of primary cancer of the gall-bladder. Two of these are mentioned by Stoll in 1777; one by Halle in 1786, and one by Baillie in 1794. All of these are included in the series collected in 1890 by Courvoisier.

During the first half of the present century but nine cases were reported, two of which were probably secondary to cancerous growths elsewhere.

The first two of these were reported in 1839 by Heyfelder, and during the same year Cruveilhier in his Pathological Anatomy mentioned the disease in speaking of the pathology of the gall-bladder, but did not go into any detailed description of the lesion.

The first full account of a case was given in 1840, by Durand-Fardel. In this the liver was not involved. Lasaze, in 1847, published a case in which also the liver was free from secondary deposits, and was not involved by continuity of growth from the gall-bladder, the most frequent way in which the disease involves neighboring parts. During the same year Notta published an account of a case.

* Osler, Wm. Lectures on Abdominal Tumors. 1894.

In 1848, Broca, and in 1849, Rippoll, each reported a case to the Anatomical Society of Paris.

The two cases that were probably secondary were that of Burridge in 1845, which is included as primary by Courvoisier, but excluded by Musser, because of cancer of the breast of some years standing, and that of Renaud in 1848.

During the next decade (1850–1860) nine cases were reported, and the literature was enriched by a number of valuable contributions. Heschl in 1852 reported a case, and refers to two others that he had seen, both of which were associated with chololithiasis. Icery and Mahieux, in 1853, each published a case. During the remaining years of this decade articles appeared, and cases were reported by Klobe, Topinard, Lebert, Pepper, Cassignac and Markham, the latter describing a remarkable case in a young woman of 28.

From 1860–1870 fifteen cases were reported. Wagner in 1863, Gull in 1864, Cornil, Foot and Stokes in 1865, reported cases, though that of the latter was probably secondary. Frarier, Lutton and Buchereau in 1866, Moxon and Paulicki in 1867, Calmetts, Murchison and Ogle in 1868, Klebs and Willigk in 1869, also reported cases.

Since 1870, the French, hitherto the chief workers in the field, have given place to the Germans, and scarcely a year has passed but some additional contribution has been made to the subject.

During 1870, Villard published the most complete paper that had as yet appeared. He was able to collect and analyze 26 cases.

Important articles have appeared at different times, in Germany, by Kohn, Kraus, Lang-Heinrich and Zenker, who reported 8 new cases and collected 28; by Bernheim and Stiller, who added 5 new cases to the list, and by Courvoisier, who devoted a chapter of his "Pathologie und Chirurgie der Gallenwege" to a summary and discussion of 103 cases.

In England, Fagge, Moxon, Habershon, and Moore have been the chief contributors, while in this country a most interesting and important paper was published in 1889, by Musser, in which he analyzes 100 cases and gives a brief synopsis of each.

Of late years the greatest interest has attached to cases of primary carcinoma of the gall-bladder, because of the association of gall-stone with a large percentage of such cases. Two views of the relation of chololithiasis to the cancer formation are held, which will be briefly discussed in another paragraph.

Symptoms.

The most important symptoms of the disease are: jaundice, presence of a tumor, pain, emaciation, vomiting and nausea, ascites, constipation or diarrhœa, loss of appetite and progressively increasing weakness.

Hemorrhages into the various tissues of the body may occur; hiccough, ptyalism and dysentery have been noted in a few cases.

Jaundice is present in a very large percentage of cases (69). It may be very slight, or progressively increasing in intensity. In a certain number it is absent. When present, it is due either to a new growth in the ducts, or occlusion of the same by stones, inflammation, or pressure from without by enlarged

glands. The skin may only present small pigmented areas, associated with more or less pronounced itching.

A tumor mass is noted very frequently. Its most frequent position is in the right hypochondrium, though it may be found occupying the area of the pylorus, or lie as low as the inguinal region. In one case it was noted in the right iliac fossa and diagnosed an ovarian cyst, the mistake being discovered upon operation.

The mass is composed either of the much enlarged gall-bladder, or more frequently of the gall-bladder and a portion of the liver attached to it.

The size may vary greatly. In some instances the whole right hypochondrium is noted as bulged, as in the first case reported this evening. The tumor may be solid or fluctuating, and at times is so movable as to have been mistaken for movable kidney.

Pain, when present, is generally complained of in the region of the liver. In the larger number of cases it is paroxysmal and lancinating in character; the paroxysms varying in duration from a few minutes to some hours. It is frequently preceded by a sensation of weight and discomfort in the right side, and is often accompanied by darting pains in the right shoulder and arm. At times it is colicky in character and complained of in the epigastric region. In certain cases the pain increases in severity and the attacks in frequency as the disease advances. Tenderness to pressure over the tumor mass is usually present, and during the attacks of pain is accentuated.

Emaciation is not as frequent a symptom as might be expected. Musser finds it in 49 cases, but considers it probably more prevalent. In a case reported by Wagner and in the first case reported this evening, the flesh was preserved.

Vomiting or nausea is present in about one half of all cases. It is occasionally obstinate and distressing. Bloody vomit has been noted.

Ascites is occasionally present and is usually accompanied by œdema of the lower extremities.

Constipation or diarrhœa is frequently noted. They occasionally alternate. In one of the cases reported constipation set in suddenly, without apparent cause, four weeks before death. Previous to this the patient had three stools a day, with a tendency to more.

Loss of appetite, usually accompanied by symptoms of indigestion and progressively increasing weakness, frequently occurs.

Hemorrhages are noted by Musser as occurring in a few cases. In two of those that I have collected they are noted; in one, into the peritoneum and body cavity; in the other, into the mucous membrane of the tongue and into the skin of the abdomen.

Fever, which is rarely noted, is never high. It usually accompanies the paroxysms of pain. I have found records of one case in which the temperature was subnormal most of the time.

With regard to sex we find, as we would naturally expect, knowing that chololithiasis is most frequent with women, that the largest percentage of cases of primary carcinoma of the gall-bladder occur among women.

In Courvoisier's cases there were four females to one male. Musser found that it occurred in the ratio of three females to one male; while the ratio 4:1 occurs in the cases that I have collected.

There is no more satisfactory explanation for the occurrence of cancer of this kind in 3 to 5 times as many women as men than there is for the more frequent appearance of chololithiasis in the female sex.

A study of the ages at which the disease is first noticed shows that it is distinctly one of middle and advanced life, or to be more accurate, of the 5th, 6th and 7th decades. By far the largest number of cases occur between 50 and 60. In Musser's table, 29 are recorded in this decade, and in Courvoisier's, 26 as against 20, the next greatest in any decade, which occurred between 60 and 70. The number gradually rises from the first decade to the sixth, and declines to the ninth. The youngest reported occurred at 4 years, in a boy, following a fall. One is reported by Mark[illegible]am, in a girl of 28, and one by Schubert, in a man of 28. [illegible]usser's table, one between 80 and 90 years is recorded, and in Courvoisier's, two.

In the cases that I have collected: one occurred between 20–30; none between 30–40; six between 40–50; nine between 50–60; four between 60–70; five between 70–80.

The duration is stated by Professor Stiller in his conclusions, drawn from the five cases that he had studied, to be between five to six years. This is distinctly at variance with the views held by other authors.

Courvoisier states that the disease is one of months, not years, and tabulates his cases as follows:

Duration 1–2 weeks, 3 cases; 3–7 weeks, 14 cases; 2–3 months, 9 cases; 3–4 months, 10 cases; 4–5 months, 3 cases; 5 months, 5 cases; 6 months, 7 cases; 7 months, 1 case; 8 months, 1 case; and summarizes, 36 of less than 4 months duration, 2 of longer than 6 months, the average being barely 3 months. Musser, on the other hand, assigns 6½ months as the average duration of the disease.

These differences of opinion can only be reconciled on the view that the different observers dated the beginning of the trouble from the appearance of different signs and symptoms.

It would seem impossible to assign any definite date for the beginning of the morbid process with anything like accuracy, because the various symptoms are known to appear at times during the progress of the disease widely different in different cases. All that we can say with confidence is that from the appearance of the symptoms the disease is one of short duration, the carcinoma developing with great rapidity.

PATHOLOGY.

As carcinoma of the gall-bladder is usually not discovered until so far advanced that such noticeable symptoms as jaundice, emaciation and pain have set in, we rarely have an opportunity to study this condition in the early stages in those who may have died from some intercurrent disease.

In such cases as come to autopsy, the gall-bladder is found to be converted in part or as a whole into a cancerous mass, usually adherent to surrounding parts, especially to the liver, duodenum and hepatic flexure of the colon. The mass is either round or pear-shaped, and in all cases where not con-

siderably dilated appears to be solid. It usually varies in size from a little above normal dimensions to as large as a child's head; the larger tumors being generally due to dilatation. It is whitish or brownish in color, has in general a firm, more or less elastic consistency when scirrhous in character, and is more soft and juicy when fungoid. As a general rule the surface is smooth, but at times it is found studded here and there with small nodules, which, according to Klebs, are secondary deposits in the overlying peritoneum.

On cutting into the mass there is found at about its center either the obliterated remains of the gall-bladder, or else its much contracted cavity, usually partly filled with a brownish fluid, sometimes purulent, and containing gall-stones or the fragments of former calculi.

The small-sized tumors are rarely made out on physical examination, while the larger ones are found either projecting below the liver border or imbedded apparently within the substance of the liver, depending, probably, on the original position of the growth; or again they are found lying under a tongue-like process of liver tissue which they have drawn down with them as they grew.

The primary position of the carcinoma may be either at the fundus or at the neck of the bladder. The position was only mentioned in twelve of Musser's cases, and occurred six times in each locality. On the other hand, Courvoisier believes that the fundus is more often the starting-point, and suggests as a reason the more constant irritation from gall-stones that would be likely to occur here.

The cancer spreads either by forming metastases in distant parts, or by continuity of growth into neighboring organs.

One form of growth by continuity is described by Courvoisier, where the neoplasm invades such distant organs as the stomach, pancreas, etc., by growing across adhesions, using them, so to speak, as bridges.

Distant organs are comparatively rarely involved by metastatic growth. The liver, however, is frequently involved in this way, the secondary deposits being generally found on or near the surface of the organ. Growth by continuity most frequently involves the liver, forming at times masses of cancerous growth much larger than the original growth in the gall-bladder. In these cases Naunyn believes that the primary growth reaches the liver probably through the bile passages (Reichert and Du Bois Raymond, Archiv, 1866, H. No. 6). Klebs suggests, on the other hand, that these may have become secondarily involved from growth in the parenchyma which has become cancerous through growth by continuity. He inclines, however, to Naunyn's view.

Willigk has reported a very interesting case in which the growth extended tree-like into the liver substance about the bile-ducts.

In most cases the growth in the gall-bladder is scirrhous in character, the walls being transformed in part or as a whole into a dense, coarse fibrous tissue, generally poor in cells, in which epithelial cells are found arranged either in solid clumps, isolated or confluent, or as alveoli and sometimes resembling the acini of glands, which may be either straight or branched. Occasionally the cells are found lying in long single rows between the fibers of connective tissue. The neoplasm is believed by many to develop either from the epithelial layer of the mucous membrane or from the glandular tissue in the mucosa. The cells are either round or cuboidal, and rarely a flat-celled growth is met with. In a number of cases in which the gall-bladder is dilated, papillary growths are found upon its inner walls that consist of solid tongues of epithelial cells, which on section may be seen running as deeply into the bladder-walls as through the muscular coat, where they often take on a glandular arrangement.

Frequently the mucous membrane is found absent in places or entirely wanting. The walls are occasionally ulcerated; where this has gone far enough, fistulous openings are formed frequently into the duodenum or transverse colon. There is in these cases generally an involvement of the intestine in the cancerous degeneration. Murchison states that of several cases of such fistula which he saw, the gall-bladder was cancerous in all but one. Degenerations occasionally occur in the cancer mass, and calcareous nodules are sometimes found.

A few pathologists, among them Förster, believe that carcinoma of the gall-bladder is in most cases secondary to a growth in the liver. This view is probably incorrect, because, as Klebs and others have pointed out, the gall-bladder is found to be uninvolved in most cases of primary liver cancer.

As to the liver itself in these cases, it is most frequently enlarged. Of the other cases, about half are atrophic and half of normal size. In a very few cases abscesses are found.

The Relation of Cholelithiasis to Primary Carcinoma of the Gall-Bladder.

Two directly opposite views are held respecting the relation of gall-stone formation to cancerous growth in the gall-bladder. According to such men as Klebs, Von Schupple, Murchison, Durand-Fardel, Krauss, Zenker and others, the new growth may be directly attributed to the prolonged irritation produced by gall-stones, especially in persons predisposed to cancer. Zenker holds that an adenoma develops by irritation, and that it changes into an adeno-carcinoma, which is the primary atypical growth. On the other hand, Lutton, Lancereaux, Lang-Heinrich, Förster and others hold that the presence of the neoplasm favors the formation of calculi, and is the cause, not the result, of gall-stone formation. It is a well recognized fact that biliary concretions are found in a very large percentage of cases of carcinoma of the gall-bladder.

In Courvoisier's list, the percentage in which stones were actually found was 91 per cent. There is good reason to believe, however, that these figures should be larger, as in a number of cases in which calculi were not found there were such evidences as scars and strictures of the ducts to show the former existence of cholelithiasis.

In Musser's cases the percentage was 92 per cent., while in those that I have collected stones were found in 20, were noted as absent in 1, and were not mentioned one way or the other in 7, making the percentage of cases with, to those without concretions, 95.4 per cent.

These figures are too great to allow us for an instant to suppose that the association of these two conditions is merely accidental. The most important point to be settled, and the

one which it seems would be conclusive, is whether the formation of gall-stones precedes or follows the cancerous degeneration.

Evidence in favor of the former view is plentiful, while that to support the latter is very meager, though there are a number of theoretical considerations used as arguments that it will lead us too far to discuss here.

I have been able to find but one case, *i. e.* that of Ord, cited by Musser, in which a calculus existed which was definitely proved to be post-cancerous in its formation, and this stone was not a cholesterin formation, but consisted of phosphate and carbonate of lime with altered mucus. On the other hand, there are numerous observations that go to prove the existence of stones prior to the carcinomatous growth.

In one of Zenker's cases, for example, fragments of calculi were found, and in the first case I have reported this evening the calculi were much disintegrated, which would seem to point to a degeneration, not to a formation of gall-stones. This fact, in connection with the long-standing history of biliary colic, is conclusive, and would lead us to believe that in all cases when there has been a previous history of biliary colic, and when no stones are found at autopsy, they have existed, but have undergone some such disintegration before the death of the patient.

Again, in one of the cases reported by Klobe an old stone was found with commencing cancer of the neck of the bladder. Klobe states it as his belief that the small size of the gall-bladder in many cases of cancer would be against the formation of calculi, while Zenker holds that the growth in the bladder and ducts would tend to prevent the bile entering the bladder, and so prevent the formation of stones.

Quetsch reported a case in which stones had been passed by a biliary cutaneous fistula for 3 years prior to any signs of cancer; and cases are reported in which stones were found although the cystic duct was occluded; they have also been found buried in the mass of the neoplasm.

From all these facts it would seem that if we are justified in ascribing a causative influence to local irritation in case of cancer in other situations, we should look upon gall-stones as exerting the same influence in these cases.

Finally, in closing, we may briefly summarize the most important points, following closely the conclusions reached by Dr. Musser, as follows:

1. Primary carcinoma of the gall-bladder is much less uncommon than was formerly believed.

2. It occurs most frequently in women, the ratio being 3–5 : 1.

3. It is a disease more particularly of the middle decade of life.

4. Gall-stones are found in from 91–95 per cent. of the cases, and probably bear a causative relation to the disease.

5. Metastasis is not extensive: invasion of neighboring organs by continuity, common.

6. Adhesions to adjacent organs frequently occur. Ulceration and perforation are more rare.

7. Pain, jaundice, cachexia, emaciation, tumor, indigestion, nausea, vomiting, constipation or diarrhœa, with occasional ascites and œdema, are the chief symptoms.

8. Pain occurs in 62 per cent. (Musser).

9. Jaundice occurs in 69 per cent. (Musser.)

10. Tumor occurs in 68 per cent. (Musser.)

11. The disease is always fatal, and usually in a short time, the average duration varying according to the best authorities from 3 to 6½ months.

12. Death is due to exhaustion, peritonitis, metastasis to other organs, and to biliary obstruction.

BIBLIOGRAPHY.

Baillie: The Morbid Anatomy of some of the most important Parts of the Human Body. London, 1793. Dtsch. v. Sommering, Berlin, 1794.

Barth et Bisnier: Art. Voies Biliaires. Dict. Encyclop. des Sc. Med.

Belcher, T. W.: Case of Cancer of the Gall-bladder and neighboring Tissues. Dublin Q. J. Med. Sc., 1861, XXXI, p. 238-240.

Belgodere, A.: Sur les Tumeurs formées par la Vésicule Biliaire. Montpellier, 1876.

Bernheim and Simon: Revue Med. de l'Est. Nancy, 1887, XIX, p. 492-500.

Bertrand: Études sur le Cancer de la Vésicule Biliaire. Paris, 1870.

Birch-Hirshfeld: Pathology, Vol. II, p. 972.

Blocq: Prog. Med., 1886, 25, IV, p. 638.

Bouchereau: Bull. Soc. Anat. de Paris, 1866, p. 191.

Bradbury: Lancet, London, 1886, I, p. 788.

Bridge: Chicago Med. Jour. and Examiner, 1887, XXXIV, p. 330.

Burhenne: Beiträge zur Statistik des Liberkrebses. Dissert., Göttingen, 1887.

Burridge, R.: Case of Scirrhus of the Gall-bladder. Prov. Med. and Sur. Jour., London, 1845, p. 734.

Callmettes: Cancer de la Vésicule Biliaire; communication avec l'Estomac, Côlon, et l'Entestine, etc. Bull. Soc. Anat., 1868, XLIII, p. 561-563.

Carre: Sur le Traitement de la Tumeur Biliaire, suivi de quelques considerations sur cette maladie. Paris, 1828.

Cassaignac: Bull. Soc. de Chir. de Paris, 1858-59, IX, 419-421.

Carrington: Trans. Path. Soc. London, 1884, p. 231.

Caubert: Cancer de la Vésicule Biliaire, etc. Bull. Soc. Anat., 1872, 1874, XLVII, p. 40.

Cénas: La Loire Medicale, 1888, 6, p. 141-146.

Chachamowicz: Ein Fall von primären Gallenblasenkrebs bei Steinbildung in der Gallenblase. Dissert., Greifswald, 1890.

Charcot: Maladies des Vieillards.

Charpentier: Presse Med. Belge, 1876, T. 28, p. 89.

Chiari, H.: Gallertcarcinom der Gallenblase nebst Cholelithiasis. Ber. d. k. k. Krankenanst. Rudolph-Stiftung in Wien (1879), 1880, p. 484.

Chouppe: Bull. Soc. Anat., 1872, p. 282.

Collinet: Bull. Soc. Anat., July 1 and 15, 1892.

Coraza: Schmidt's Jahrbücher, 1873, Bd. 160.

Cornil and Charcot: Mem. de l'Acad. de Med., T. XXVII, p. 349.

Cornil and Ranvier: Manuel d'Histologie Pathologique, T. II.

Corraza: Bull. Soc. Med. di Bologna, Serie 5a, T. 12, 1871, p. 123.

Corvisart: Bull. Soc. Anat., 1848, p. 43.

Cossy: Bull. Soc. Anat., 1878, LIII, p. 462.

Coupland, S.: Primary Cancer of the Gall-bladder. Tr. Path. Soc. Lond., 1879-80, XXXI, p. 136-138.

Cruveilhier: Traité d'Anat. Path. Gen., II, pp. 542 and 543.

Courvoisier: Kasuistische-statistische Beiträge zur Pathologie und Chirurgie der Gallenwege. Leipzig, 1890.

Cowy: Progrès Med. Paris, 1879, VII, p. 205.

Delageniere: De la Cholicystenterostomie. Thèse, Paris, 1890.

Denucé: Tumeurs et Calcules de la Vésicule Biliaire. Thèse, Agreg. Paris, 1886.

De Vincentis: Resoc. Acad. Med. Chir. de Napoli, 1878, XXXII, p. 107-120.

Dupré, E.: Des Infections Biliaires. Étude bactériologique et clinique. Thèse, Paris, 1890.

Durand-Fardel: Bull. Soc. Anat., 1838, XIII, p. 157-160.

Eustache: Jour. Med. Sc. de Lille, March 20, 1884, anne. 7, No. 6.

Fagge: Guy's Hosp. Reports, 1875, XX, 3rd series, p. 167.

Fazio, F.: Giorn. Internaz. d. Sc. Med., 9, 1887, p. 385-397.

Foot, A.: Cancer of the Gall-bladder. Dub. Q. J. M. Sc., 1865, XXXIX, p. 218.

Förster: Path. Anat., II, p. 206.

Frarier; Bull. Soc. Anat., 1866, p. 56-59.

Frerichs: Traité pratique des Maladies du Foie, p. 661.

Funccius: Ueber Gallensteinen und ihre Folgen. Dissert., Bonn, 1873.

Gerstang: Lancet, 1888, II, p. 963.

Goodhart: Atlas of Illust. Path. Syd. Soc. Pub., 1882.

Gull: Lancet, London, 1864, I, p. 699.

Haas: Prager Vtel. J. Schrift. Ber. üb. med. Klinik. v. Jaksch, 1874-75, Bd. 132, p. 136-137.

Habershon: British Medical Journal, 1872.

Habershon: Some Diseases of the Liver. Philadelphia, 1872.

Hallé: Hist. de la Soc. de Med., 1786 (Paris, 1790), p. 125.

Hanot et Gilbert: Études sur les Maladies du Foie, 1888.
Hauteville: Des Tumeurs formées par la Vésicule Biliaire. Thèse, Paris, 1873.
Hayem: Villard's Synop. Table.
Hein: Ber. d. k. k. Krankenanst. Rudolph-Stiftung in Wien (1881), 1882, p. 294.
Heitler: Wiener med. Wochenschr., 1883, No. 32, p. 989.
Henrot: Bull. Soc. Med. de Reims., 1874, XIII, p. 23-33.
Heyfelder: Archiv Gen. de Med., 1839, T. 6, p. 444-446.
Heschl: Ein Fall von Zottenkrebs der Gallenblase. Ztschr. d. k. k. Gesellsch. d. Aerzte zu Wien, 1852, II, p. 251.
Icery: Cancer de la Vésicule Biliaire. Bull. Soc. Anat., 1853, XXVIII, p. 73-76.
Kiemann: Ber. d. k. k. Krankenanst. Rudolph-Stiftung in Wien (1879), 1880, p. 339.
Klebs: Handbuch der path. Anat., Berlin, 1869.
Klobe, J.: Ueber Zottenkrebs der Gallenblase. Wchndl. d. k. k. Gesellsch. d. Aerzte zu Wien, 1856, II, p. 749-753.
Kocher: Orig. K. Gesch. Inselspital, Bern, 1888.
Koch, G.: Ein Fall von Carcinom der Gallenblase. Ber. klin. Wochenschr., 1880, XVII, p. 196-198.
Kohn: Der primäre Krebs der Gallenblase. Dissert, Breslau, 1879.
Krauss, J.: Deutsch. Archiv f. klin. Med., 1884, Bd. 34, p. 270.
Lacaze: Bull. Soc. Anat., 1847, p. 355.
Lambl: Virchow's Archiv, 1855.
Lancereaux: Traité d'Anat. Path., T. I, p. 410 et 455.
Lancereaux: Sémain Médicale. 7, 1887, p. 334.
Landau: Movable Kidney. Syd. Soc. Pub., 1889, CX, p. 325.
Lang-Heinrich: Vier Fälle von Gallenblasencarcinom. Halle, 1881.
Lebert: Traité d'Anat. Path., etc., Paris, 1857, T. II, p. 325.
Lermoyez: Le Prog. Médical, 1884, p. 1095.
Leroux, H.: Progres Médical, 1880, VIII, p. 390.
Leuf: Proc. Med. Soc. Kings Co., N. Y., 1883, VIII, p. 291.
Liebman, C.: Carcinoma della Cistifellea. Rosoconto Sanitano dell 'Osp. Civ. di Trieste, 1876, 1-4, p. 211.
Littré: Dict. de Med., T. V, 2nd edition.
Loomis, H. P.: Medical Record, N. Y., May 10, 1890.
Lutton: Nouveau Dict. de Med. and de Chir. Pratique, 1866, V. 54.
Mahieux: Bull. Soc. Anat., 1853, p. 180.
Marchand, F.: Deutsch. med. Wochen., 1888, XII, p. 221.
Markham: Tr. Path. Soc. London, 1856-57, VIII, p. 243.
Martin: Ber. klin. Wochen., 1879, No. 22 u. 23.
Martius: Ueber primären Krebs d. Gallenblase. München, 1891.
Moor, N.: Tr. Path. Soc. London, 1879-1880, XIII, p. 138.
Mears: Tr. Amer. Surg. Assn., 1889.
Morin: Contribution a l'Étude d'Epitheliome primitif de la Vésicule Biliaire. Thèse, Paris, 1891.
Moxon: Tr. Path. Soc. London, 1867, XVIII, p. 140-142.
Mulot: Bull. Soc. Anat., 1882, LVII, p. 171-175.
Murchison; Lectures on Diseases of the Liver, etc. London, 1868, p. 540, case XCVI, and p. 543-545.
Muschold: Dissert., Berlin, 1876.
Musser, J. H.: Tr. Assn. Amer. Physicians, 1889; also Phil. Med. Times, 1880-81, XI, p. 730-732.
Naunyn: Klinik der Cholelithiasis, 1892, p. 153.
Niemeyer, E.: Beitrag z. Kasuistik d. Geschwülste d. Gallenblase u. d. Gallenwege. Dissert., Würzburg, 1888.
Notta: Bull. Soc. Anat., 1847, XXII, p. 335-337.
Oettinger: Prog. Med., 1885, 25, I, p. 414.
Osler, J. W.: St. George's Hospital Reports, 1868.
Osler and Bell: Canada Med. and Surg. Journal, April, 1877.
Owen, I.: St. George's Hospital Reports, 1879, X, p. 35.
Path. Inst. Basel: A. S., 325, 1874, sect. 105; 1882, sect. 156; 1882, sect. 328; 1888, sect. 8; 1883, sect. 291; 1884, sect. 257; 1886, sect. 290; 1888, sect. 85.
Paulicki, A.: Carcinom d. Gallenblase. Ber. klin. Woch., 1867, IV, 348.
Pepper, W.: Am. Jour. Med. Sc., Phila., 1857, n. s., XXXIII, p. 13-25.
Pertik: Owösi Hetilap. Pest. Med.-Chir. Presse, 1885, XXI, p. 157.
Peters, H.: Dissert., Kiel, 1890.
Phillipp: Dissert., Greifswald, 1888, p. 10-21.
Planteau: Bull. Soc. Anat., 1875, I, p. 689-692.
Prompt: Bull. Soc. Anat., 1866, XLI, p. 374-376.
Quetsch: Ber. klin. Wochenschr., 1885, No. 42.
Quinlan: British Medical Journal, Feb. 28, 1874.
Ramon: Cronica Medico-Quir. de la Habana, 1879, V, p. 81.
Remy: Bull. Soc. Anat., 1885, p. 203-205.
Renaud: London Medical Gazette, 1848, n. s. VI, p. 340.
Rickards: Lancet, London, 1872, II, p. 559.
Riedel: Berlin klin. Wochen., 1888, No. 30, p. 603.
Rippoll: Bull. Soc. Anat., 1849, XXIV, p. 359.
Robertson and Fitzgerald: Australian Med. Journal, 1871, n. s. 9, p. 221-223.
Rokitansky: Path. Anat., Syd. Soc. Translation, Vol. II, 161.
Salisbury, J. H.: Chicago Med. Jour. and Examiner, 1879, XXXIX, p. 29-31.
Schmidt's Jahrbücher, 1873, Bd. 160, p. 74.
Schmidt, F.: Ein Fall v. primären Gallenblasenkrebs. Dissert., Kiel, 1891.
Schreiber: Ber. klin. Wochen., 1877, No. 31.
Schrotter: Bericht. d. k. k. Allgemeinen Krankenhauses zu Wien, 1881-1882, p. 23.
Schueppel, V.: Ziemssen, Vol. VIII, Krankheit d. Gallenwege, p. 68.
Smith, P.: Tr. Path. Soc. London, 1865-66, XVII, p. 465.
Smith, W. G.: Tr. Royal Ac. Med. in Ireland, 1888, VI, p. 367-369.
Socin: Orig. K. Gesch. Chir. Abtheg. Spital, Basel, 1889.
Spohr, R.: Ein Beitrag zur Pathogenese des Gallenblasenkrebses. Dissert., Giessen, 1892.
Stiller, B.: Pester Med. Chir. Presse, Nos. 35-38, 1886.
Stokes: Dublin Q. J. Med. Sc., 1865, XXXIX, p. 218.
Stoll: Ratio-Medendi, Wien, 1777, Ps. I, p. 290.
Tiedmann: Zur Kasuistik des primären Gallenblasenkrebses. Dissert., Kiel, 1891.
Topinard: Société Anat., 1856, p. 239.
Tyson, J.: Phila. Med. Times, 1873-74, IV, p. 652.
Villard: Bull. Soc. Anat., 1870, p. 217.
Voss: Norsh. Mag. f. Lägend, Bd. XXIV, p. 167.
Walshe: Nature and Treatment of Cancer. London, 1846, p. 331.
Wagner, E.: Primärer Krebs der Gallenblase. Archiv d. Heilk., Leipzig, 1863, IV, p. 184.
Weber, W.: Dissert., Würzburg, 1891.
Wells, T. S.: Lond. Med. Times and Gazette, 1878, I, p. 671.
Wigglesworth: Medico-Chir. Journal, 1887, VII, p. 217.
Williglk, A.: Virchow's Archives, 1869, Bd. XLVIII, p. 524.
Zenker: Deutsches Archiv für klinische Medicin, Bd. 44, 1889, p. 159.

PROCEEDINGS OF SOCIETIES.

THE JOHNS HOPKINS HOSPITAL MEDICAL SOCIETY.

Meeting of April 2d, 1894.

Dr. KELLY in the chair.

Myoma complicating Pregnancy and preventing Delivery.—Porro-Cæsarean Operation modified by dropping the Pedicle.—DR. KELLY.

This patient is presented before the Society this evening, as she leaves the hospital in a short time, and I wish to review briefly the case, especially the reasons for submitting her to Cæsarean Section.

She was referred by her physician to the Johns Hopkins Hospital in the seventh month of her pregnancy, with the statement that she had a fibroid tumor preventing delivery.

Examination revealed a myoma about the size of a large orange springing from the posterior wall of the cervix, and two of smaller size on the anterior wall of the fundus. The cervical tumor blocked the inferior strait, preventing delivery of the fœtus, and was so closely wedged into the pelvis as to render myomectomy, craniotomy, or its displacement upward impossible, and thus there was but one other measure to be considered, that of Cæsarean Section.

The date of her confinement was calculated as nearly as possible, this being rather difficult to determine accurately on account of the irregular menstruation occasioned by the myomata, and she was submitted to operation near her full term.

The preparations for operation were the same as for ordinary cœliotomy. The abdominal incision was made from above the symphysis to a short distance above the umbilicus, and the uterus delivered upon the abdomen. In opening the uterus I cut through one of the myomata and the hemorrhage at first was quite profuse.

The child was rapidly delivered, and the cord was immediately clamped with artery forceps and cut. In the meantime Dr. Russell controlled the hemorrhage by grasping the cervix below the tumor.

As the danger of subsequent hemorrhage in these myomatous uteri is very great I determined to do a Porro-Cæsarean operation, modified by dropping the pedicle. Accordingly I introduced tem-

porary sutures through the uterine incision to control the slight tendency to hemorrhage at this point, and proceeded with the hysterectomy according to the method which I have adopted for the removal of large myomatous uteri.

The ovarian and uterine arteries were ligated on either side and the uterus amputated below the cervical tumor.

The flaps of the uterine stump were then accurately approximated with silk sutures, covered with peritoneum and dropped back into the pelvis. The abdominal incision was closed with buried silk sutures and the skin approximated with a subcutaneous silk suture. No drainage.

The patient leaves for home to-morrow, four weeks from the time of operation, having had an uncomplicated convalescence and now feels perfectly well. The baby died the night following the operation and the autopsy revealed atelectasis of the bases of both lungs.

Infusion of Normal Saline Solution in connection with Gynecological Operations and the Accidental Hemorrhages of Parturition.—DR. KELLY.

During the past year I have employed infusion of normal salt solution a number of times in patients *in extremis* and I am certain that it has proved a life-saving measure in at least four cases.

The liability to hemorrhage in gynecological operations, especially in certain classes of pelvic diseases, is probably greater than in any other branch of surgery.

The blood-vessels of the pelvic organs are subject to the most varied distribution and displacement as a result of inflammatory disease and the growth of tumors, and when the tumor is a rapidly growing one and during pregnancy, the vessels often become very much enlarged and engorged. In some cases the vessels are exposed with the greatest difficulty, and the patient may lose a large amount of blood before the bleeding vessel can be reached and controlled.

In the hemorrhage of parturition, either ante- or post-partum, this measure is undoubtedly of the greatest service, and I am certain that were it more generally employed by the general practitioners of our country the rate of mortality from post-partum hemorrhage would greatly be reduced. The first occasion on which I employed infusion, with signal success, occurred in an obstetrical case. I was called to see the patient one evening and found her complaining of vague pains which lacked the force and regularity of those of normal labor. The nurse called my attention to the fact that the patient had passed a small quantity of blood, and on examination I found a large clot in the vagina.

Fœtal heart-sounds which had been present up to a short time before the beginning of labor were now absent. At first I suspected placenta prævia, but upon closer examination was unable to detect any evidence of this anomaly, and therefore concluded that it was a case of concealed hemorrhage. Proceeding upon this assumption I performed version and rapidly delivered the dead fœtus.

The amount of blood which poured from the uterus was enormous, and no one but a very strong and plethoric woman could have withstood such extreme depletion.

Never before have I seen a patient recover from such a hemorrhage. The pulse became very rapid and soon reached 160.

As there was still slight hemorrhage and the patient continued to have the severest cramp-like pains, I called assistants about five hours after the child was delivered, and after a careful examination under chloroform a piece of the placenta was found at the fundus uteri. The patient's pulse was now imperceptible and we resorted at once to infusion, following the plan suggested by Dr. Clark, which is simply a reversal of the ordinary use of the aspirator.

The receiving-bottle of the aspirater was filled about two-thirds full of normal salt solution (.6 per cent.) at a temperature of 105° F., the air-pump was reversed, forcing air into instead of exhausting air from the bottle, after which the stop-cock was closed and the bottle inverted. While an assistant was preparing the apparatus for infusion I exposed the radial artery by a short oblique incision.

I prefer arterial infusion, as the dangers from the entrance of air are less and the beneficial result more immediate than when a vein is employed for this purpose.

Before opening the artery two provisional ligatures should be passed beneath the artery, one above and one below the point of infusion.

After making a longitudinal slit in the artery the exit stop-cock was opened and the solution was allowed to flow before introducing the blunt needle of the aspirator into the artery; in this way all possible danger of the entrance of air is avoided. In this case there was not the slightest bleeding on opening the artery, the pulse having been imperceptible for some minutes. About one litre of fluid was infused and the effect was remarkable; hardly had the salt solution begun to flow when the pulse of the opposite wrist became perceptible and within a short time dropped to 125 and became quite full in volume. The convalescence in this case, although slow, was perfectly satisfactory.

Only one other instance of concealed hemorrhage occurring during parturition and treated by transfusion is reported.*

In many of its details this case of Dr. Taylor, reported in the London Lancet, is similar to the one which I have just presented to you.

He was called to see a woman who was supposed to be sinking during a protracted labor. The patient's pulse was nearly imperceptible, extremities cold, and she presented all of the symptoms of profuse hemorrhage.

Examination revealed the same condition as I have just described in my case, with the exception that the membranes were partially protruding. Uterine action had ceased and no effort was made to deliver the fœtus, but resuscitative measures were at once instituted.

About ten ounces of blood were transfused from the patient's sister, a strongly-built young Irish girl. The immediate effect of the transfusion was not so gratifying as in the case which I have just detailed, but on the whole her recovery was very satisfactory. The patient was delivered of a dead fœtus about twelve hours after the transfusion.

The results of infusion in three of my surgical cases have been no less gratifying.

In April, 1893, I removed the appendages of one side for a hæmatoma of the ovary in a young woman. During the afternoon of the same day her pulse suddenly began to increase in rapidity and soon all the signs of hemorrhage became pronounced.

I reopened the abdomen and found the pelvis filled with blood and active hemorrhage still continuing—the result of a ligature slipping from the ovarian artery. While I caught and religated the bleeding vessel, Dr. Russell transfused about one pint of salt solution. In this case the pulse quickly dropped from 150 to 130 and the patient made an uninterrupted recovery.

The second case was the one of which I spoke at a previous meeting of the Society.

This patient was already excessively anæmic from profuse hemorrhage, due to carcinoma uteri, and during my attempts to perform abdominal hysterectomy the bleeding became so profuse that I was compelled to ligate both internal iliac arteries. In this case 800 cc. of salt solution were infused.

In my last case profuse hemorrhage occurred the day after vaginal hysterectomy for carcinoma, and before it was arrested the patient had become pallid, was exceedingly restless, tossing from one side of the bed to the other, expression anxious and air hunger very pressing. The radial pulse had also disappeared in this case when the needle was introduced.

The results in these four cases have been very gratifying, and I feel that in all cases where hemorrhage has been so profuse as to

* Taylor, London Lancet, Vol. LXXII, p. 159.

threaten life no time should be lost in at once resorting to transfusion.

The method just detailed is simple, and if properly carried out perfectly safe, and by its employment we give the patient the benefit of the slightest chance for recovery.

I would especially advise arterial infusion, as it is certainly less dangerous and the immediate stimulating effect is much more marked. The rapid gain in the volume of the pulse on the opposite side is not due to the blood being forced back into the heart, but to the simple fact of resistance being supplied to the heart. The fluid is forced back to the first branches of the artery and thence gains access to the main circulation by passing through the capillaries. In this way the mixture of the blood and salt solution is more gradual than when the latter is at once thrown into the venous circulation and carried directly to the heart.

According to my judgment one or two and probably all of the patients just spoken of would have died had not infusion been employed.

Exhibition of Surgical Cases.—Dr. Finney.

Appendicitis.—In the absence of Dr. Halsted I will show some of the final results in cases operated on for appendicitis in the Johns Hopkins Hospital. We sent word to all of the living cases asking them to come here to-night, but only seven have responded.

Since the Hospital was opened, 35 cases in all have been operated on: 30 males, 5 females; 27 were adults, 7 children; 25 cases recovered, 10 died. Operated during the first attack, 19; during some recurrent attack, 8; between attacks, 6. The appendix was removed wholly or in part in 24 cases, and abscess of the appendix was simply opened in 11 cases. There was general suppurative peritonitis present in 8 cases, and of those cases in which there was a record of the bacteriological examination of the pus, in 7 a pure culture of the colon bacillus was found, in 2 the green pus organism and in 2 pure cultures of streptococcus. There were 8 cases operated upon with general purulent peritonitis, all of which resulted fatally. All of these 8 cases were *in extremis* when operated upon, and of only one had we any hopes of recovery; that one lived a week. It was a case of pure colon bacillus infection. The other 2 deaths were both cases in which a simple abscess had been opened. The one died on the second day from pneumonia with an acute nephritis complicating. The other case died on the fourth day with chronic nephritis; the patient died in a comatose condition, and the autopsy revealed very small contracted kidneys. The latter was the oldest case operated upon, a man 72 years of age. The youngest was a boy aged 12.

Reviewing the cases hurriedly, we find representatives of almost every possible variation. They all gave, at the onset, a more or less typical history, suggesting possible trouble in the appendix; later on other symptoms developed. One of the fatal cases had been treated by his family physician for 5 days for bladder trouble on account of difficulty in micturition. He had shown symptoms that undoubtedly suggested appendicular trouble, but they had been overlooked, and the one prominent symptom of difficulty in micturition had attracted attention. When the patient arrived at the Hospital he was in a very bad way; the abscess had ruptured, and there was a general peritonitis. This was a case in which the green pus organism was found. In two cases the abscess was located in the left iliac region instead of in the right. In neither had the disease been at first diagnosed, and when they reached the Hospital, one was almost moribund and the other extremely ill. Both were operated upon, and in each a general purulent peritonitis was found. We found that in each case there was an unusually long appendix, which had extended directly across to the left of the median line, just at the brim of the pelvis. The tip had been in each case the starting-point of the trouble. In the one it was gangrenous, in the other there was a perforation. Both cases terminated fatally. They were treated as are all the cases of general peritonitis, by as thorough cleansing of the peritoneal cavity as possible through the primary lateral incision, and later, if necessary, through a median incision. This cleansing process was done quickly, and the cavity drained with iodoform gauze. One of these cases was thought to be a case of volvulus, since the trouble had been located in the region of the sigmoid flexure and there had been absolute constipation for 4 or 5 days previous. In another case the abscess was situated so high up on the right side, and so close under the edge of the liver that it was impossible to differentiate it from liver abscess, although it was supposed to be a case of appendicitis at the time of the operation. In another case there was gangrene of the entire cæcum. In this case there was also a general peritonitis. The man was very septic at the time of operation and soon succumbed. In still another case, the abscess cavity was extra-peritoneal at the time of admission to the hospital. Most of the swelling was below Poupart's ligament. The operation showed that the appendix had been shut off from the peritoneal cavity, and that the abscess had begun to burrow down the front of the thigh, in much the same way that a psoas abscess does. This case recovered. Another was one of so-called catarrhal appendicitis, pure and simple. It was the case of my roommate at college, whom I had watched for a long time. There was at no time any marked rise of temperature or tumor, but there was always a tenderness over the appendix, so much so that he was incapacitated for work. He came into the hospital at my suggestion and the appendix was removed by Dr. Halsted. He recovered and is perfectly well at this date, three years later.

These cases illustrate very well different types of the disease, from the simple catarrhal variety, to gangrene of the entire cæcum; simulating a liver abscess, a twist of the sigmoid, or a psoas abscess covering pretty much the whole abdomen, and giving a wide latitude for differential diagnosis.

As far as the operation itself is concerned, we believe in operating in all cases in which there is definite indication of the existence of an inflammation of the appendix, with the following exceptions. If it is at the end of an attack, and there is given the history of preceding attacks, we rather advise waiting until this attack has subsided, operating in the interval. If it is the first attack, and a mild one, other things being equal, it is advised to wait until further developments. Of the six cases operated upon between attacks, all recovered, and in none of them at the present time is there a hernia. During the operation we isolate as much as possible the general peritoneal cavity from the seat of the trouble, by packing it off with sterilized gauze, or, in some cases, where there is considerable pus, with iodoform gauze. Of course, if there is one large pus cavity, that is simply drained, and unless the appendix presents in the wound, there is no attempt made to remove it. If there is only a little pus and the appendix can be found, which sometimes is a very difficult matter, it is separated from the adhesions and removed. A strip of iodoform gauze is inserted about the stump and brought out of the wound. Of course there is great objection to leaving the abdominal wound open, as there is always danger of a subsequent hernia, but this method seems to give the best results up to the present time.

Those of you who care to, may examine the results in the seven cases who are present. There is nothing to be seen, as you will observe, except in this man, who was operated upon about 15 months ago and the appendix removed. He now has a marked bulging of the scar almost as large as my fist. It gives him no inconvenience and he does heavy work right along. He has worn no abdominal support, contrary to our advice. In one of the other cases there is a slight impulse on coughing. I am sorry I cannot give a report on all the cases as to the existence of hernia.

Dr. Osler.—What is the objection to closing the wound in these instances of appendicitis unless there is extensive suppuration? I know a case of a physician in New York who has been much troubled after an appendix operation by just such a condition as was present in one of the cases shown here, namely, a very large hernia associated with which is a great deal of colic, possibly

due to adhesions. If I understood him aright, his appendicitis was one without general suppuration, but it had been treated by the open method, and a very large hernia had developed in a very short time.

DR. FINNEY.—I do not know that there is any objection in certain cases. The reason heretofore given for the open method has been fear of our inability to sufficiently disinfect the abscess cavity or the region about the stump. I believe that in many cases it is possible to so thoroughly disinfect this as to render it innocuous, and I propose when the next favorable opportunity presents, to close the wound tightly. A sufficient number of cases has been reported, I think, to justify such a procedure in selected cases.

Injury to the Shoulder.—This man, who applied to the surgical dispensary for treatment to-day, illustrates a very interesting form of injury to the shoulder-joint, the pathology of which I cannot satisfactorily explain. There is no description of this particular injury in any of the modern text-books, so far as I am aware. It is in our experience in the dispensary, one of the commonest injuries met with in the shoulder-joint. It is brought about in a variety of ways. We have observed it following direct violence, for example a blow or fall, striking on the shoulder, or indirectly following heavy lifting or carrying heavy weights on the shoulder, etc. Ten days ago this man fell a few feet, striking on his elbow. Since that time he has been unable to do any work by reason of the intense pain produced by motion of the arm. The condition is this: you cannot see any difference between the two shoulders on inspection. On palpation you will not feel anything different, unless occasionally a slight joint crepitus; but you will notice an exquisitely tender point just beneath the coracoid process, and at times tenderness at a corresponding point on the posterior aspect of the shoulder. There is always a disinclination to move the arm; it hangs as if paralyzed. You can raise it without much difficulty to the horizontal position; bringing it forward while held horizontally is the motion that produces the greatest pain. When you let go of the arm it drops as if helpless. Dr. Thomas has examined a number of these cases and has found nothing abnormal in the innervation. There seems to be no especial tenderness along the course of any of the nerves or muscles, unless possibly over the short head of the biceps. Limited motion of the arm in any direction is attended by very slight pain. The joint itself, except at the points noted, is not sensitive to pressure. The treatment is quite satisfactory. The Paquelin cautery, applied daily, usually relieves the pain and brings back the motion of the arm in a very short time, in the recent cases. In the older cases the relief is not so rapid. The arm should be kept at rest for a few days.

Meeting of May 7, 1894.

The Lesions caused by certain so-called Toxalbumins.—DR. FLEXNER.

The crystalline principles called ptomaines which have been isolated by Selmi, Nencki, Brieger and others, from cultures of bacteria do not, as was once supposed, represent the essentially active agents produced by pathogenic bacteria. Since the isolation of a poisonous albuminous principle from cultures of the bacillus diphtheriæ by Roux and Yersin in 1888, a number of albuminous substances have been obtained from pathogenic bacteria. The researches of Kobert, Stillman, Martin and Hellin have resulted in the separation from the castor bean and the jequirity bean of two amorphous substances, ricin and abrin, which in many respects resemble the toxic albuminous principles obtained from bacteria. We owe to Weir Mitchell and Reichert our knowledge that the toxicity of snake venom depends upon certain albuminous constituents, and Mosso and Springfeld found an exquisitely poisonous substance in the blood of eels. Moreover, the well-known effects which the blood of one species of animal exerts upon another species had led to the belief that the blood of different animals contains distinctly toxic substances. As to the precise nature of these substances, to which the name of toxalbumins has been provisionally given, there is little agreement. By some authorities they are regarded as enzymes, while a few deny altogether their albuminous nature.

The experiments which I wish to report to you briefly this evening consist of the study of the effects of some of these toxic albuminous substances upon animals, especially upon guinea-pigs, rabbits and mice. As has been indicated, the bodies derived from the several sources mentioned seem to possess certain chemical properties in common, and in considering their pathological action we shall find reason to treat them together. In considering for a moment the production of immunity, which, for many bacteria and their products, is an established fact, we find that evidence is not wanting for the toxalbumins derived from the higher plants, the phytalbumoses, whereas up to the present time no one has succeeded in rendering animals durably immune from the animal toxic proteids, although Sewall claims to have secured in pigeons an immunity from snake poison, which, however, disappeared after a time.

Ehrlich has shown us that mice, which are relatively quite susceptible to ricin and abrin, can be rendered in a high degree immune from the action of these bodies. I have repeated Ehrlich's experiments and confirmed his results; and I have found, in addition, that immune mice which resist large doses of the drug when introduced subcutaneously, may still succumb to a similar quantity injected into the peritoneal cavity.

Having in mind the production of immunity to this substance, I have experimented on rabbits with dog's serum, but so far without success. On the contrary, I found that animals which had withstood one dose of dog's serum would succumb to a second dose given after the lapse of some days, or weeks, even when the dose was sublethal for a control animal.

The pathological lesions produced in animals by these various poisonous substances have been very imperfectly studied up to the present time. The contributions refer almost exclusively to the gross changes in organs and tissues, or consider simply the effect which is produced upon the blood, especially the alterations in coagulability. In the case of ricin or abrin poisoning, the pathological changes have been considered to depend upon an active gastro-enteritis, thrombosis of vessels in the stomach and intestine followed by necrosis and ulceration from digestion. Just as little attention has been given to the tissue changes caused by the inoculation of foreign serum into animals. Heretofore it has sufficed to consider as the cause of death in the immediately fatal cases, the coagulation of the blood, especially in the right heart and main pulmonary vessels, or the production of widespread capillary thrombosis. All experimenters have, however, been confronted with cases in which, as death has been delayed for several days, this explanation was insufficient, since thrombi were not demonstrable. Ponfick, however, has shown that the kidneys suffer injury in excreting the hæmoglobin liberated by the breaking up of the red blood corpuscles, and he attributes many cases of death to the resulting nephritis and blocking of the tubules with met-hæmoglobin casts. The microscopical study of the pathological changes in the organs has convinced me of the insufficiency of these views, and the extent and not the absence of tissue alterations is most remarkable.

Some three years ago Professor Welch and myself published a short communication on the lesions produced in the tissues by the soluble products of the diphtheria bacilli. This paper, following one describing the histological lesions in kittens, guinea-pigs and rabbits caused by the inoculation of the bacilli themselves, confirmed in all essential respects the first paper. These lesions are found extensively in the tissues, and are present in the lymphatic glands generally, in the spleen, liver, intestinal canal, kidneys and heart muscle. They are characterized, moreover, by a death of cells in the affected part, and they exhibit a decided tendency to occur in well-marked areas or foci, indicating that soluble sub-

stances circulating in the blood are capable of producing focal lesions.

With a view of testing further the production of focal changes in the tissues by the use of soluble poisons, I employed ricin and abrin. These substances, as already pointed out, resemble in many ways the bacterial poisons. One of the impressive results in their use was the certainty of their action. Kobert showed that 0.03 mg. per kilogram of ricin was fatal to rabbits, cats and dogs, and Ehrlich's experiments indicated that guinea-pigs were so susceptible that one gram of the substance would suffice to kill no less than 1,500,000 of these animals. Up to the present time I have experimented upon mice, guinea-pigs and rabbits with these bodies and among my experimental animals I have had acute and chronic cases. The acute cases present such a characteristic picture that it is unmistakable.

The intravenous inoculation of ricin dissolved in 10 per cent. salt solution in the proportion of 0.3 mg. to 3 mg. per kilogram of weight kills rabbits in from 18 to 26 hours. The lymphatic glands generally are found swollen, œdematous and congested. The intestines are distended with fæces resembling cholera stools, and the patches of Peyer are greatly swollen and often hemorrhagic. The spleen is much enlarged, the kidneys congested, and the liver, besides being congested, presents foci to the naked eye of yellowish or yellowish-white color, which at times are surrrounded by hemorrhagic zones.

The microscopical changes were marked. In the lymph glands besides congested vessels and hemorrhages, many of the lymphatic elements were destroyed. Cells with fragmented nuclei were abundant and karyokinetic figures numerous. The lymphatic tissue of the intestines showed in an analogous manner the destructive action of the poison, and the spleen was affected in a manner similar to the lymph glands. The liver presented a variety of forms of cell death. The endothelium of the capillaries was sometimes necrotic, and the leucocytes in the vessels were often destroyed. The liver-cells in the yellowish or yellowish-white foci mentioned were necrotic, sometimes hyaline, or very pale and vacuolated, the nuclei not uncommonly having suffered fragmentation. Again, the liver-cells were converted into a reticulated structure resembling fibrin, and indeed the foci often gave a reaction with Weigert's fibrin-stain. In these organs the lesions tend to occur in distinct foci, and the areas of necrosis attract polynuclear leucocytes in considerable numbers.

We now know that certain stimuli of a chemical nature attract and repel leucocytes as well as other cells. In undergoing necrosis certain chemical changes take place in the tissues through which the leucocytes are attracted to them, but some bacterial products are still more positively chemotactic than are these substances derived from cells. Capillary tubes were filled with solutions of ricin in normal salt solution of varying strengths, 1 to 100,000, 1 to 200,000, 1 to 500,000 and 1 to 1,000,000, and introduced beneath the skin of rabbits. Control tubes of physiological salt solution were also introduced. After 20 hours the ricin solution of 1 to 100,000 proved to be strongly chemotactic. The weaker solutions exhibited positively chemotactic properties directly in proportion to the concentration.

Chronic ricin poisoning is associated with great disturbance of nutrition. There are wasting and evidence of great blood destruction. The kidneys in such a case exhibited atrophic patches.

I have also studied the lesions caused by the blood serum of one animal when introduced in another species of animal. Thus far my studies have been confined to the action of the blood serum of man and dogs upon rabbits. The inoculated animals, as often happens, may succumb immediately, in consequence of thrombosis of the right side of the heart, the respiratory function ceasing before the heart's action. Not uncommonly the animal experiences less severe effects, and after a variable period of depression, increased frequency of respiration, weakness and hæmoglobinuria, apparently recovers. I have found dog's serum strongly globulicidal for rabbits. Doses of 1.5 per cent. of body weight were usually fatal, sometimes immediately, at others after 10 to 12 hours. Quantities of 1 per cent. caused profound disturbances, in rare instances death, while some animals appear to recover. In the last series death may occur after several days or weeks. These cases are of especial interest as lesions are found in the tissues. While the observations which I have made are more complete as regards the action of the serum of the dog upon rabbits, the serum derived from human beings apparently acts in much the same way. These lesions resemble, but are not identical with those described in connection with the toxalbumins of diphtheria, ricin and abrin.

In the acute cases degeneration of the epithelium associated with the presence of met-hæmoglobin casts are found in the kidneys. The spleen shows a tolerably rich fragmentation of nuclei and necrosis of cells situated especially in the malpighian bodies, and the liver contains foci of necrosis of liver cells. Of especial interest is an animal which died on the 13th day. At the autopsy emaciation was marked; the peritoneum contained an excess of fluid, the axillary glands were enlarged, the intestinal lymphatic apparatus apparently normal. The liver, which was firm in consistence, was roughened externally and dark in color. The kidneys appeared small, the capsule was not adherent, but the surface was granular. In the spleen were a number of white wedge-shaped areas, the bases at the capsule. Attached to the chordæ tendinæ of the tricuspid valve was a calcified thrombus as large as a split pea. The urine contained albumin and casts. The microscopical changes were those of chronic interstitial processes in the liver and kidneys, while the wedge-shaped masses in the spleen looked like healed infarctions. In the liver the chronic changes were best studied and their relation to degeneration and necrosis of cells was evident.

In rabbits which died at a somewhat earlier period, after 5 to 6 days, I have found coagulation necrosis of liver cells. To these areas leucocytes are not attracted in such very large numbers, and in keeping with this I have found that capillary tubes containing dog's serum, when introduced beneath the skin of rabbits and removed after 26 hours, showed slight positive chemotaxis only.

In the end the differences in the action upon the tissues of the toxic agents discussed are not so great as their correspondences, a fact which emphasizes their chemical similarity. They so affect the tissue elements as to cause degeneration and death, and are followed by reparative processes which do not restore the integrity of the tissues. And, from this study of the changes in the tissues, we have seen that acute degenerative lesions, focal in character, may be produced by soluble poisons, and these be followed by proliferation of the connective tissue of the parts, leading to chronic interstitial changes in the internal organs.

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